EXHIBIT A





**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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|---|---|
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| EXAMINER: | Fubara, Blessing M. |
| APPLICANT: | Cherukuri, Subraman Rao |
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| FOR: | DRUG DELIVERY SYSTEMS |

**AMENDMENT/RESPONSE**

**CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8**

DATE OF DEPOSIT:
March 29, 2006

I hereby certify that this paper or fee (along with any paper or fee referred to as being attached or enclosed) is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated above and is addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Judy Anderson

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**RESPONSE UNDER 37 C.F.R. § 1.111**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Office Action mailed September 30, 2005, please enter the amendments and remarks provided below and reconsider the patent application in view thereof. A Request for Continued Examination (RCE), a petition for a three month extension of time, the appropriate fees, and an affidavit under 35 C.F.R 1.132 are enclosed herewith.

**AMENDMENT TO THE CLAIMS**

1. (currently amended) A pharmaceutical product in a compressed tablet or caplet form having a diameter and length of from about 1 mm to about 7 mm each, comprising:

a) a therapeutically-effective amount of a uniformly distributed pharmaceutical selected from the group consisting of: antibiotics, antiinfectives, cardiovascular therapeutics, gastrointestinal agents, psychotropics and mixtures thereof;

b) at least one compressible material selected from the group consisting of calcium phosphate, compressible sugar product, celluloses, polyols, and mixtures thereof;

c) at least one lubricating material in an amount of up to about 5% by weight of the product, selected from the group consisting of fats, emulsifiers, waxes, magnesium stearate, calcium stearate, talc, starches, silicon dioxide, and mixtures thereof said product being strong enough to withstand mechanical pressure and release the pharmaceutical in the gastrointestinal tract of a subject to which the product is administered.

~~; and~~

~~d) wherein said product is in the form of a caplet having a diameter from about 1 millimeter to about 7 millimeters and a length from about 1 millimeter to about 7 millimeters.~~

2. (canceled)

3. (currently amended) The pharmaceutical product of claim ~~2~~1 wherein ~~the~~ pharmaceutical is a psychotropic.

4. (previously presented) The pharmaceutical product of claim 3, wherein said psychotropic is a anti-anxiety therapeutic.

5. (previously presented) The pharmaceutical product of claim 3, wherein said psychotropic is an insomnia therapeutic.

6. (previously presented) The pharmaceutical product of claim 3, wherein said psychotropic is an antidepressant.

7. (previously presented) The pharmaceutical product of claim 6, wherein said antidepressant is selected from the group consisting of Fluoxetine HCl, Paroxetine HCl, Sertraline HCl, and Venlafaxine HCl, Amitriptyline, Nortriptyline, Imipramine, Desipramine, Doxepin, Trimipramine, Clomipramine, Protriptyline, Amoxapine, Maprotiline, Phenelzine, Tranylcypromine, Fluvoxamine, Venlfaxine, Trazodone, Nefazondone, Mirtazapine, Bupropion, or mixtures thereof.

8. (withdrawn) The encapsulated product of claim 7, wherein said pharmaceutical is Fluoxetine HCl.

9. (withdrawn) The encapsulated product of claim 2, wherein said pharmaceutical is a gastrointestinal therapeutic.

10. (withdrawn) The encapsulated product of claim 9, wherein said gastrointestinal therapeutic is a ulcer therapeutic.

11. (withdrawn) The encapsulated product of claim 10, wherein said ulcer therapeutic is selected from the group consisting of Omeprazole, Lansoprazole, Ranitidine HCl, Famotidine, Nizatidine, Teprenone, Cimetidine, Rabeprazole sodium, Sulpiride, or mixtures thereof.

12. (withdrawn) The encapsulated product of claim 11, wherein said ulcer therapeutic is Omeprazole.

13. (withdrawn) The encapsulated product of claim 9, wherein said gastrointestinal therapeutic is a anti-emetic.

14. (withdrawn) The encapsulated product of claim 13, wherein said anti-emetic is selected from the group consisting of Ondansetron HCl, Granisetron HCl,

dimenhydrinate, Tropisetron, Dolasetron mesylate, Cisapride, Sulfasalazine, Balsalazide, Infliximab, or mixtures thereof.

15. (withdrawn) The encapsulated product of claim 14, wherein said anti-emetic is dimenhydrinate.

16. (withdrawn) The encapsulated product of claim 9, wherein said gastrointestinal therapeutic is a anti-diarrheal therapeutic.

17. (withdrawn) The encapsulated product of claim 16, wherein said anti-diarrheal therapeutic is selected from the group consisting of Loperamide HCl, diphenoxylate, codeine phosphate, camphorated opium tincture, or mixtures thereof.

18. (withdrawn) The encapsulated product of claim 17, wherein said anti-diarrheal therapeutic is Loperamide HCl.

19. (withdrawn) The encapsulated product of claim 2, wherein said pharmaceutical is a migraine therapeutic.

20. (withdrawn) The encapsulated product of claim 19, wherein said migraine therapeutic is selected from the group consisting of sumatriptan succinate, amitripyline, methysergide, propranolol, valproate, verapamil, dihydroergotamine, ergotamine, metoclopramide, naratriptan, prochlorperazine, rizatriptan benzoate, zolmitriptan, eletriptan, acetaminophen, aspirin, NSAID's, opioids, or mixtures thereof.

21. (withdrawn) The encapsulated product of claim 20, wherein said migraine therapeutic is sumatriptan succinate.

22. (withdrawn) The encapsulated product of claim 2, wherein said pharmaceutical is a therapeutic for the treatment of hypertension.

23. (withdrawn) The encapsulated product of claim 22, wherein said therapeutic is selected from the group consisting of nifedipine, amlodipine besylate, losartan potassium, lisinopril, felodipine, benazepril HCl, ramipril, irbesartan, verapamil HCl, bisoprolol fumarate and hydrochlorothiazide, amlodipine and benazepril HCl, clonidine, candesartan, cilexetil, diltiazem, nicardipine, imidapril, trandolapril, eprosartan mesylate, nilvadipine, verapamil HCl, temocapril, prazosin HCl, isradipine, cilazapril, celiprolol, bisoprolol, betazolol HCl, ramipril, nisoldipine, lisinopril, trandolapril, and nisoldipine.

24. (withdrawn) The encapsulated product of claim 23, wherein said therapeutic is nifedipine.

**REMARKS**

In the Office Action mailed September 30, 2005, Claims 1, and 3-7 are pending in the present application. Claim 2 has been canceled and claims 8-24 have been withdrawn. Each of these claims was rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,197,828 to Jerussi et al. (hereinafter 'the 828 patent").

By the present amendment, Claim 1 has been amended to include several new elements. The claim now requires that the therapeutically-effective amount of pharmaceutical be uniformly distributed and be selected from the group of pharmaceutical agents consisting of antibiotics, antiinfectives, cardiovascular therapeutics, gastrointestinal agents, pschotropics, and mixtures thereof. Support for this amendment can be found in originally filed claim 2 as well as in the published original specification ¶¶ 45, and 94. Claim 1 has further been amended so as to incorporate a specific group of compressible material for use in the pharmaceutical product. Support for this amendment can be found in ¶¶ 69-70 of the published application. An additional limitation was amended into claim 1 such that the lubricating material is present in an amount of up to 5% by weight of the product and the lubricating material was selected from the group consisting of fats, emulsifiers, waxes, magnesium stearate, calcium stearate, talc, starches, silicon dioxide, and mixtures there of. Support for this amendment can be found in the published specification in ¶ 71. Claim 1 was also amended so as to require that eh product be strong enough to withstand mechanical pressure and release the pharmaceutical in the gastrolintestinal tract of the subject to which the product is administered. Support for this amendment can be found in ¶ 94.

The above-recited rejection will be addressed below. It is respectfully requested that the Examiner further consider the application in view of these remarks.

*The Present Invention*

Before discussing each of the rejections a brief summary of the present invention is made. The present invention is drawn to pharmaceutical product in a compressed tablet or caplet form having a diameter and length of from about 1 mm to about 7mm each. The pharmaceutical product comprises a therapeutically effective amount of a uniformly distributed pharmaceutical, at least one compressible material,

and at least one lubricating material. The lubricating material can be present in the product in amounts of up to 5% and the product as a whole must be able to withstand mechanical pressure and release the pharmaceutical in the gastrointestinal tract of the subject.

*Rejections Under 35 U.S.C. § 103*

The Examiner has rejected claims 1-7, under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. '828 patent. The Applicant respectfully submits that these claims are patentable over the cited reference for the reasons set forth below, and that the rejection should be withdrawn.

As has been discussed in the previous responses, the '828 patent discloses methods of preparing, and compositions comprising derivatives of (+) venlafaxine. The dosage forms may include tablets, caplets, troches, lozenges, dispersions, suspensions, suppositories, ointments cataplasms, pastes, powders, dressings, creams, plasters, solutions, capsules, soft elastic gelatin capsules, and patches. The only teaching specifically regarding compressed tablet or caplet formulations is found in Example 7, beginning at the bottom of column 26 and running through column 27. Table III sets for the formulations for the compressed tables. For ease of reference, Table III of the '828 patent has been recreated below. It is noted that the final two rows of the recreated table are added and contain the total weight of each capsule and the percent of lubricant (lubricant as used in the pending claim 1) per capsule.

**TABLE III of '828 patent**

| Compressed Tablet Unit Dosage Forms | | | |
|---|---|---|---|
| Component | 25 mg capsule | 50 mg capsule | 100 mg capsule |
| (+)-O-desmethyl-venlafaxine | 25 | 50 | 100 |
| Microcrystalline Cellulose | 90.0 | 90.0 | 90 |
| Pre-gelatinized Starch | 100.3 | 97.8 | 82.8 |
| Croscarmellous | 7.0 | 7.0 | 7.0 |
| Magnesium Stearate | 0.2 | 0.2 | 0.2 |
| Total Weight | 222.5 | 245 | 280 |
| % Lubricant* | 45.17% | 40.0% | 29.64% |

* Calculated by dividing the sum of the weights of Magnesium Stearate and the pre-gelatinized starch by the total weight of each formulation.

As shown in the table above, the compressed oral formulations of '828 patent contain a pharmaceutical in the form of venlafaxine, a compressible material in the form of microcrystalline cellulose, and lubricating materials in the forms of pre-gelatinized starch and magnesium stearate. However, there is no teaching in the '828 patent that the lubricating material be limited to "up to about 5%" of the total weight of the pharmaceutical product, as required by claim 1 of the pending application. As shown in the table above, the compressed oral formulations taught by the '828 patent contain at least 29% by weight of a lubricating material as defined in claim 1 of the present invention which is contrary to the teachings of the teachings of the present claims and application. Additionally, there is no teaching or suggestion in the '828 patent that limiting the amount of the lubricating material to 5% or less would be desirable. Therefore the '828 patent does not teach each and every element of the claimed invention.

The formulations of the '828 patent further fail to teach a tablet which is compressible into a diameter and length of from about 1mm to about 7mm. The Examiner has previously stated that size of the pharmaceutical product alone would not be sufficient to render the present invention patentable. The Applicant does not argue that the size alone is what renders the present invention patentable, but rather the formulation itself, which renders the pharmaceutical product capable of being compressed into the claimed sizes. As stated in the previously submitted affidavit, which is resubmitted herewith, the formulations of the '828 patent are not capable of being compressed into tablets or caplets as required by the claims.

As provided in the Declaration, applicant tried but was unable to make a tablet of 9mm size by following the '828 patent disclosure of columns 26 and 27. The dry blend powder could not be compressed and remained as a powder. Applicant then conducted three additional experiments to improve upon the '828 patent disclosure so that a pharmaceutically acceptable tablet of 9mm size could be produced. In experiment 2, applicant tried to granulate the product in an effort to improve compressibility. Again, applicant could not compress the granules into a tablet. In Experiment 3, applicant used talc to improve compressibility and hardness. However the product was still unsatisfactory. Applicant then conducted Experiment 4 whereby more talc was used. In Experiment 4, the product was compressible and of suitable hardness. Applicant studied the '828 patent with regard to the formulation used in

Experiment 4 and determined that there was teaching of such a formulation. The formulation of Experiment 4 did not exhibit a controlled release profile, specifically because 90% or more of the drug was released within the first hour.

As the '828 patent fails to teach a pharmaceutical formulation with 5% or less of a lubricating material and a formulation which can be compressed into a tablet or caplet with a size of from about 1mm to about 7mm, it fails to teach each and every element of the pending claims. As such, it is respectfully requested that the rejection be withdrawn and the pending claims allowed.

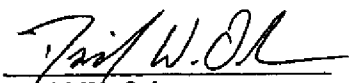
## CONCLUSION

In view of the foregoing, Applicants believe that pending claims 1-7 present allowable subject matter and allowance thereof is respectfully requested. If any impediment to the allowance of these claims remains after consideration of the above remarks, and such impediment could be removed during a telephone interview, the Examiner is invited to telephone the undersigned attorney at (801) 566-6633 so that such issues may be resolved as expeditiously as possible.

Please charge any additional fees except for Issue Fee or credit any overpayment to Deposit Account No. 20-0100.

Dated this 29th day of March, 2006.

Respectfully submitted,



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**STATEMENT OF THE SUBSTANCE OF THE INTERVIEW**

An in-person interview was held with Examiner Fubara and Applicant's representatives, Dr. Phanesh Koneru and Mr. David Osborne on February 23, 2006. During the interview the testing procedures carried out and presented in Applicant's declaration filed as part of the previous office action response were discussed. It was also discussed that it had been discovered that a page of the declaration had been inadvertently missing, potentially causing the Examiner's previous confusion.

It was agreed that Applicant would file a new copy of the complete declaration with the next office action response. Further it was agreed that Applicant would amend Claim 1 to place the size range of the claimed tablet in the preamble, and recite some of the additional claim components in markush lists of preferred agents.